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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,673	03/23/2005	Tatsuo Hoshino	K21409USWO C038435/018565	2412

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EXAMINER	
RAGHU, GANAPATHIRAM	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
03/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,673	HOSHINO ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-18* is/are pending in the application.

4a) Of the above claim(s) *3,4,9-12,14,15,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6-8, 13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

In response to the Office Action mailed on 05/11/09, applicants' response and amendments received on 11/13/09 is acknowledged. Said amendment, amended claims 1, 2, 6, 8, 13 and 16. Thus, Claims 1-4 and 6-18 are pending in the application. Claims 3, 4, 9-12, 14-15 and 18 remain withdrawn as they are drawn to non-elected inventions. Claims 1, 2, 6-8, 13 and 16 are now under consideration for examination.

Withdrawn-Claim Rejections: 35 USC § 112, second paragraph

Previous rejection of claims 1, 2, 6, 7 and 13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is being withdrawn in view of the amendments to the claims.

Withdrawn- New Matter-Claim Rejections 35 USC § 112, first paragraph

Previous rejection of claims 1, 2, 8 and claims 6, 7, 13 and 16 depending therefrom rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement/New-matter, is being withdrawn, in view of the amendments to the claims.

Withdrawn-Rejections 35 USC § 112, first paragraph

Previous rejection of claims 1, 2, 8 and claims 6, 7, 13 and 16 depending therefrom rejected under 35 U.S.C. 112, first paragraph, for enablement, is being withdrawn in view of the amendments to the claims.

Withdrawn-Claim Rejections 35 USC § 112, first paragraph

Previous rejection of claims 8 and 16 depending therefrom rejected under 35 U.S.C. 112, first paragraph, for enablement/Biologic-deposit, is being withdrawn in view of the Exhibit 1 and persuasive arguments **(page 18 of applicants' remarks dated 11/13/09)**.

Reinstated-Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-8, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Asakura et al., (EPO 832974 A2, date of publication 01/04/1998) when given the broadest interpretation. Claims 1, 2, 6-8, 13 and 16 are directed to a process for the production of L-ascorbic acid comprising: contacting an enzyme with a substrate selected from the group consisting of, L-gulose, L-galactose, L-idose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid, L-idono-1,4-lactone, L-idonic acid, L-talono-1,4-lactone and L-talonic acid, wherein said enzyme has the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence 90% identical to SEQ ID NO: 2 thereto, with the activity to produce L-ascorbic acid (claims 1-2) and to a process for producing L-ascorbic acid comprising contacting a substrate which is selected from L-gulose, L-galactose, L-idose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid with Enzyme B of *G.oxydans* DSM 4025 and isolating L-ascorbic acid from the reaction, wherein Enzyme B has the following physico-chemical properties: a) molecular weight of about 60, 000 Da on SDS-PAGE; b) substrate specificity for primary and secondary alcohols and aldehydes; c) pH stability at a pH of about 6 to about 9; d) pH optimum of about 8.0; and e) inhibited by Cu^{2+}, Zn^{2+}, Mn^{2+}, $Fe^{2+}$and Fe^{3+} under specific defined process conditions such as pH,

temperature and time in which the substrates are allowed to react with said enzyme (claims 5-8, 13 and 16).

Asakura et al., (*supra)* disclose the purification, kinetic profiles and physico-chemical characterization of a polypeptide designated as Enzyme B from *G.oxydans* DSM 4025 that has 100% sequence homology to SEQ ID NO: 2 of the instant application with identical physico-chemical properties and substrate specificity for primary and secondary alcohols, optimal pH range, pH stability, thermal stability and effect of metals and inhibitors on the activity of said enzyme (Table: 1, 2, 3, 4 and 5) and host cells transformed with polynucleotide encoding said polypeptide and examiner takes the position that the reference enzyme inherently has all the biochemical properties as the polypeptide of the instant invention. Furthermore, Table 10, page 23 discloses L-idose as a substrate for Enzyme B and the formation of L-idonic acid and the use of said enzyme in a process for the production of L-ascorbic acid and the intermediates of L-ascorbic acid (Abstract section). The claims as written "A process for production of L-ascorbic acid comprising: is interpreted as "open language" and therefore the process for production of L-ascorbic acid can comprise other elements in the reaction and hence reads on the disclosure of Asakura et al. Furthermore, neither the claims as written nor the specification explicitly states that the said process for the production of L-ascorbic acid is a direct one step-conversion of claimed substrates into L-ascorbic acid. The said process of L-ascorbic acid was carried out under specific cellular context, i.e., production of L-ascorbic acid in a process comprising: contacting an enzyme having the amino acid sequence of SEQ ID NO: 2 encoded by a

polynucleotide of SEQ ID NO: 1, said polypeptide expressed in a specific strain of *E.coli* JM 109 having the activity to produce L-ascorbic acid from substrates L-gulono-1,4-lactone/L-gulonic acid from L-gulose and from L-galactono-1,4-lactone/L-galctonic acid or conversion of substrate L-galactose to L-galactono-1,4-lactone/L-galactonic acid and L-ascorbic acid under suitable culture conditions (as in Examples: 1-3, pages 8-10; and culture conditions: lines 15-28, page 6 of specification) and therefore said bacteria may provide other necessary enzymes either for the production of intermediate products of L-ascorbic with claimed substrates or for the final conversion of the intermediate products to L-ascorbic acid.

Therefore the reference of Asakura et al., (EPO 832974 A2, date of publication 01/04/1998), is deemed to anticipate claims 1, 2, 6-8, 13 and 16 as written.

Reinstated-Claim Rejections: 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 6-8, 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asakura et al., (EPO 832974 A2, date of publication 01/04/1998) and further in view of Bourdant et al., (Enzyme Micro. Technol., 1990, Vol. 12, pages 322-329) and Hancock et al., (TRENDS in Biotechnol., 2002, Vol. 20 No. 7, pages 299-305).

Claims 1-2, 5-8, 13 and 16 are directed to a process for the production of L-ascorbic acid comprising: contacting an enzyme with a substrate selected from the group consisting of L-gulose, L-galactose, L-idose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid, L-idono-1,4-lactone, L-idonic acid, L-talono-1,4-lactone and L-talonic acid, wherein said enzyme has the amino acid sequence of SEQ ID NO: 2 or an amino acid sequence 90% identical to SEQ ID NO: 2 thereto, with the activity to produce L-ascorbic acid under specific defined process conditions such as pH, temperature and time in which the substrates are allowed to react with said enzyme.

Asakura et al., (*supra*) teach the purification, kinetic profiles and physico-chemical characterization of a polypeptide designated as Enzyme B from *G.oxydans* DSM 4025 that has 100% sequence homology to SEQ ID NO: 2 of the instant application with identical physico-chemical properties and substrate specificity (as discussed in 102 (b) rejection above). However, said reference is silent regarding the some of the substrates selected from the group L-gulose, L-galactose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid, L-idono-1,4-lactone, L-talono-1,4-lactone and L-talonic acid.

Bourdant et al., and Hancock et al., (*supra*) teach the different processes and conditions for the production of L-ascorbic acid, such as The Reichstein process, Bacterial fermentation processes and the different pathways, substrates and products such as L-sorbose, L-gulonic acid, L-idonic acid to 2,keto-L-gulonic acid or 2,keto-L-

idonic acid utilized by bacteria and the enzymes produced by the bacteria in the production of L-ascorbic acid (entire document).

The instant application relates to a process of production of L-ascorbic acid comprising: contacting an enzyme with a substrate selected from the group consisting of, L-gulose, L-galactose, L-idose, L-talose, L-gulono-1,4-lactone, L-gulonic acid, L-galactono-1,4-lactone, L-galactonic acid, L-idono-1,4-lactone, L-idonic acid, L-talono-1,4-lactone and L-talonic acid. The claims as written "comprising" is interpreted as "open language" and therefore 1) the process may involve additional enzymes or processes to produce the final product L-ascorbic acid and nowhere in any of the claims is it explicitly stated that the claimed process is a one-step process for the production of L-ascorbic acid; and 2) only support in the specification for production of L-ascorbic acid is a process comprising: contacting an enzyme having the amino acid sequence of SEQ ID NO: 2 encoded by a polynucleotide of SEQ ID NO: 1, said polypeptide expressed in a specific strain of *E.coli* JM 109 having the activity to produce L-ascorbic acid from substrates L-gulono-1,4-lactone/L-gulonic acid from L-gulose and from L-galactono-1,4-lactone/L-galctonic acid or conversion of substrate L-galactose to L-galactono-1,4-lactone/L-galactonic acid and L-ascorbic acid under suitable culture conditions (as in Examples: 1-4, pages 8-10; and culture conditions: lines 15-28, page 6 of specification) and said bacterial strain is interpreted to comprise many other enzymes that are involved in the conversion of other claimed substrates into intermediates, said intermediates are acted upon by enzyme having the amino acid sequence of SEQ ID NO: 2 encoded by a polynucleotide of SEQ ID NO: 1 to form L-ascorbic acid.

Combining the teachings of the above references, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to develop a process for the production of L-ascorbic acid using the enzyme taught by Asakura et al., wherein they disclose the different substrates and intermediate products made by Enzyme B from *G.oxydans* DSM 4025 including the substrate L-idose and intermediate product L-idonic acid and further suggest enzyme's use in L-ascorbic acid synthesis. One of ordinary skill in the art would have been motivated to make or use such an enzyme in the production of L-ascorbic acid and one of ordinary skill in the art would have had a reasonable expectation of success, since the references of Bourdant et al., and Hancock et al., (*supra*) teach the various pathways and a list of intermediates and substrates that can be employed for the production of L-ascorbic acid, further strengthening the motivation and reasonable expectation of success to use Enzyme B of *G.oxydans* DSM 4025 with the substrates disclosed in the present invention for the production of L-ascorbic acid.

Therefore, the above references render claims 1, 2, 6-8, 13 and 16 *prima facie* obvious to one of ordinary skill in the art.

Reasons for reinstatement of withdrawn rejections was explicitly provided in the Final-Office-Action dated 02/01/2008 and is enclosed in the instant Office-action as a ready reference (pages 9-10 of the Final-Office-Action dated 02/01/2008).

Withdrawn-Claim Rejections 35 USC § 102

Previous rejection of claims 1-2, 6-8, 13 and 16 under 35 U.S.C. 102(b) as being anticipated by Asakura et al., (EPO 832974 A2, date of publication 01/04/1998) is being withdrawn. Amendment to claims has necessitated the withdrawal of the instant rejection. However, examiner for the record would like to state that if the "new-matter" is cancelled by the applicants, the rejection will be reinstated and such an action by the examiner will not be considered as new ground of rejection.

Withdrawn- Claim Rejections 35 USC § 103

Previous rejection of claims 1, 2, 6-8, 13 and 16 under 35 U.S.C. 103(a) as being unpatentable over Asakura et al., (EPO 832974 A2, date of publication 01/04/1998) and further in view of Bourdant et al., (Enzyme Micro. Technol., 1990, Vol. 12, pages 322-329) and Hancock et al., (TRENDS in Biotechnol., 2002, Vol. 20 No. 7, pages 299-305) is being withdrawn. Amendment to claims has necessitated the withdrawal of the instant rejection. However, examiner for the record would like to state that if the "new-matter" is cancelled by the applicants, the rejection will be reinstated and such an action by the examiner will not be considered as new ground of rejection.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1. Claims 1, 2, 6-8, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Asakura et al., (EPO 832974 A2, date of publication 01/04/1998) when given the broadest interpretation.

2. Claims 1, 2, 6-8, 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asakura et al., (EPO 832974 A2, date of publication 01/04/1998)

and further in view of Bourdant et al., (Enzyme Micro. Technol., 1990, Vol. 12, pages 322-329) and Hancock et al., (TRENDS in Biotechnol., 2002, Vol. 20 No. 7, pages 299-305).

Allowable Subject Matter/Conclusion

None of the claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652